Diabetic Kidney Disease:

An Update

Hussein Sheashaa, MD

Professor of Nephrology, Urology and Nephrology Center and Director of Medical E-Learning Unit, Mansoura University and Executive Director of ESNT- Virtual Academy: http://lms.mans.edu.eg/esnt/

MNDU, Feb 6th , 2015

Continuous Glucose Monitoring

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FDA News Release

FDA permits marketing of first system of mobile medical apps for continuous glucose monitoring

Data-sharing capability allows caregivers to monitor patient's blood sugar levels remotely

For Immediate Release: January 23, 2015

Summary: The U.S. Food and Drug Administration today allowed marketing of the first set of mobile medical apps that allow people with diabetes to automatically and securely share data from a continuous glucose monitor (CGM) with other people in real-time using an Apple mobile device such as an iPhone.

Inquiries

Media

Jenny Haliski
301-796-0776

Consumers

888-INFO-FDA

Share

121

Glucose Monitoring

Seminars in Dialysis

HEMOGLOBIN A1C IN THE ESRD POPULATION

Hemoglobin A1c in the ESRD Population: Status Report

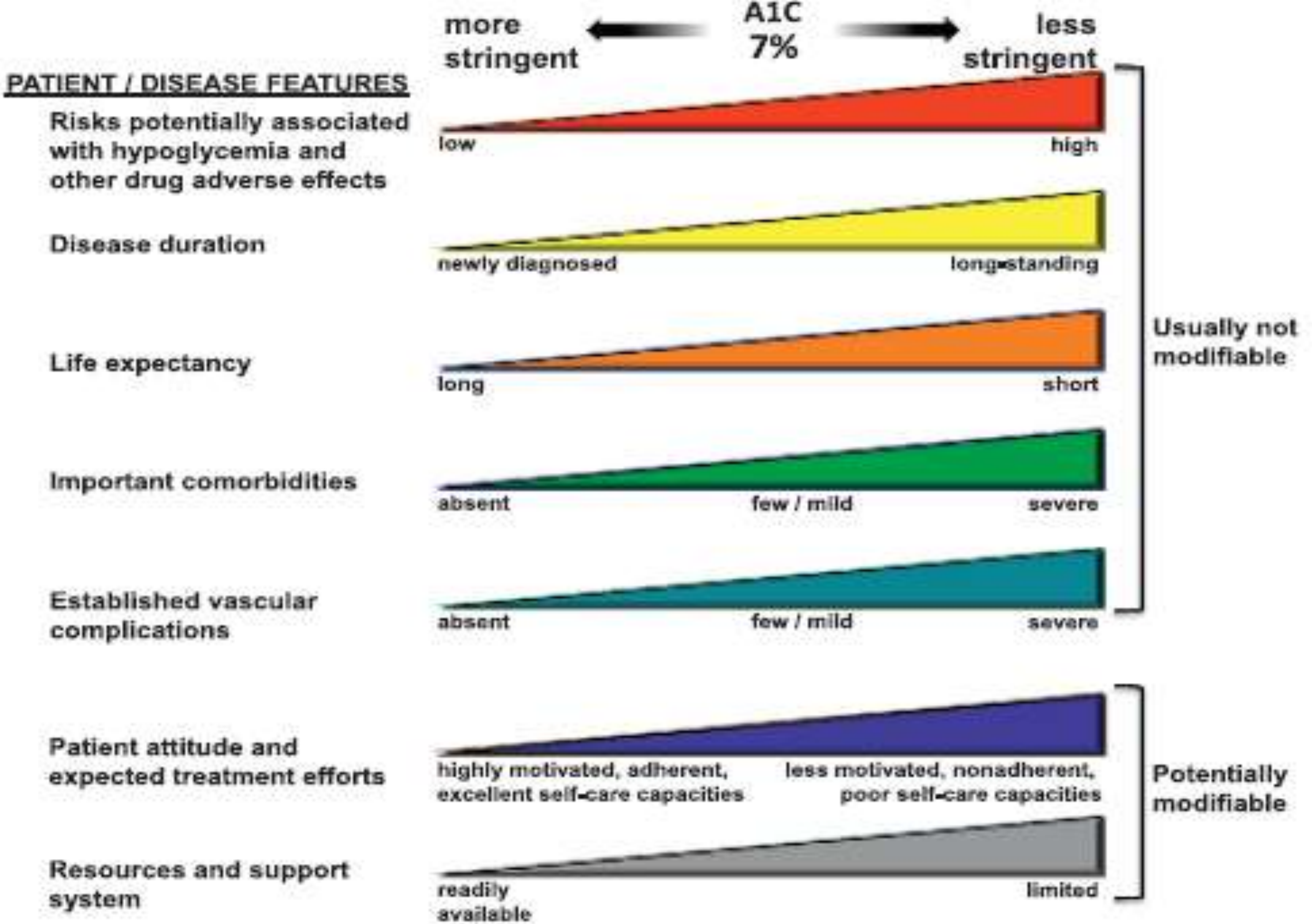
Mark E. Williams
Joslin Diabetes Center, Harvard Medical School, Boston, Massachusetts

Hemoglobin A1c: key features in ESRD vs. general population

- Weaker correlation with serum glucose levels
- HbA1c values may be relatively low, influenced by ESAs, anemia, and iron administration
- Limited correlation with patient outcomes

Seminars in Dialysis

November–December 2014
Volume 27, Issue 6
Pages 537–648, E55–E70



Diabetes Care Volume 38, Supplement 1, January 2015

Biomarkers:
Progression of DKD (T2D)

Biomarker	Urine	Plasma	Category
Vascular endothelial growth factor A (VEGF-A)	x	x	Angiogenesis
Fibronectin	x		Fibrosis
Matrix metalloproteinase-7 (MMP-7)	x		Fibrosis
Collagen IV	x		Fibrosis
High molecular weight (HMW) Collagen IV	x		Fibrosis
Connective tissue growth factor (CTGF)	x		Fibrosis
Cystatin C	x	x	Glomerular filtration (plasma) tubular function (urine)
Nephrin	x		Glomerular injury
Podocalyxin	x		Glomerular injury
Soluble tumor necrosis factor receptor 1 (sTNF R1)	x	x	Inflammation
Soluble tumor necrosis factor receptor 2 (sTNF R2)	x		Inflammation
Monocyte chemotactic protein 1 (MCP-1)	x	x	Inflammation
Tenascin C	x		Inflammation
Fibroblast growth factor-23 C-terminus (FGF 23)	x	x	Mineral metabolism
Beta-2 microglobulin (B2M	x	x	Tubular function
Neutrophil gelatinase-associated lipocalcin (NGAL)	x	x	Tubulointerstitial injury
Liver-type fatty acid-binding protein (L-FABP)	x		Tubulointerstitial injury

eGFR: FGF-23 (OR: 2)
ESRD: VEGF (OR: 1.44)

Nephrol Dial Transplant (2014) 29: 2293–2302

Biomarkers:
Progression of DKD (T1D)

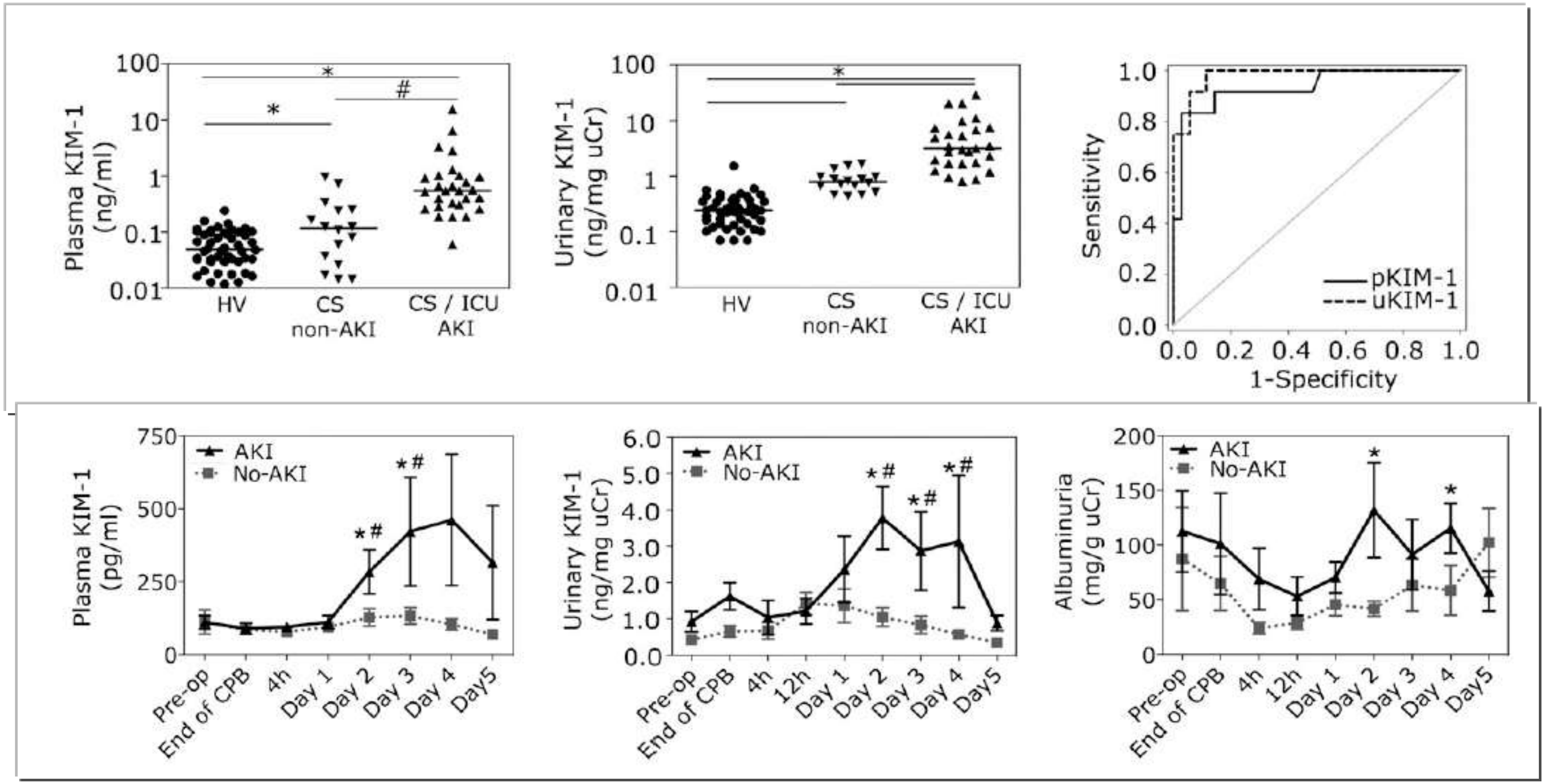
BRIEF COMMUNICATION www.jasn.org

Blood Kidney Injury Molecule-1 Is a Biomarker of Acute and Chronic Kidney Injury and Predicts Progression to ESRD in Type I Diabetes

Venkata S. Sabbisetti,* Sushrut S. Waikar,* Daniel J. Antoine,† Adam Smiles,‡ Chang Wang,* Abinaya Ravisankar,* Kazumi Ito,* Sahil Sharma,* Swetha Ramadesikan,* Michelle Lee,§ Rebeccah Briskin,§ Philip L. De Jager,§ Thanh Thu Ngo,* Mark Radlinski,* James W. Dear,‖ Kevin B. Park,† Rebecca Betensky,¶ Andrzej S. Krolewski,‡ and Joseph V. Bonventre*

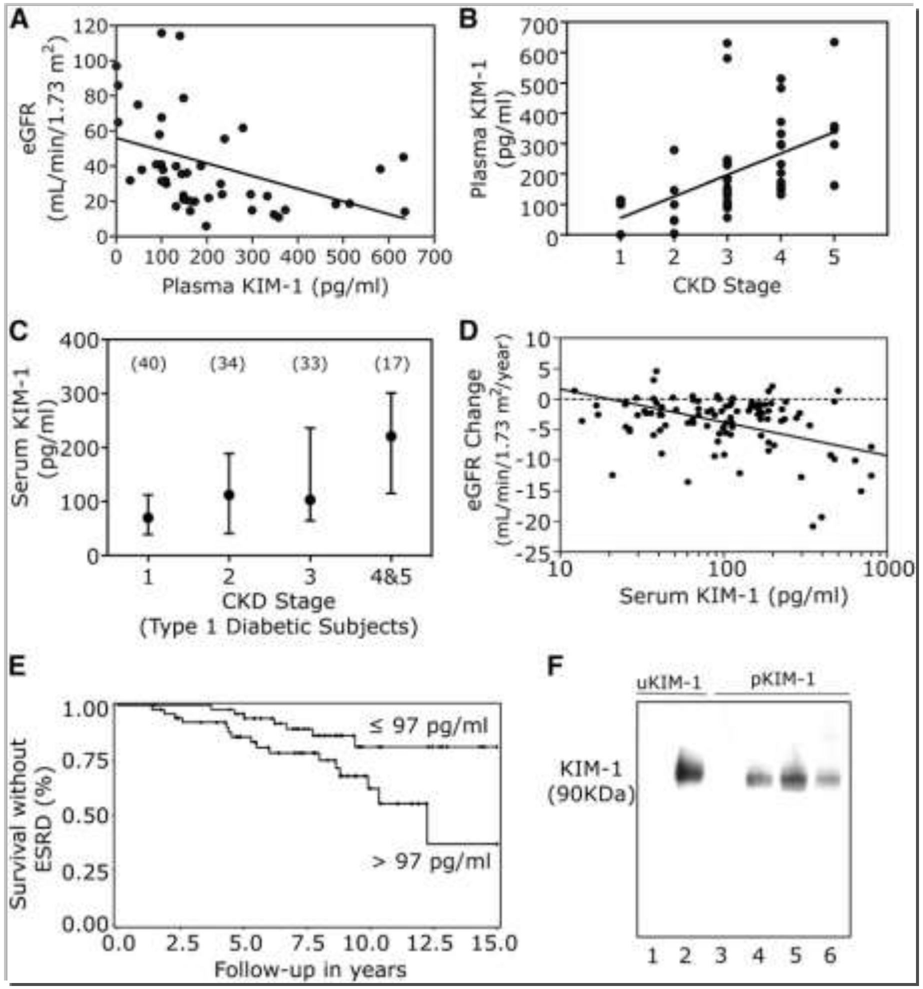
J Am Soc Nephrol 25: 2177–2186, 2014.

Biomarkers:
Progression of DKD (T1D)



J Am Soc Nephrol 25: 2177–2186, 2014.

Biomarkers:
Progression of DKD (T1D)



J Am Soc Nephrol 25: 2177–2186, 2014.

Biomarkers:
Progression of DKD (T1D)

Characteristic	Healthy Volunteers (*n*=48)	CS Patients without AKI (*n*=16)	CS/ICU Patients with AKI (*n*=28)
Age (yr)	34±1	74±2	74±2
Men, *n* (%)	24 (50)	10 (63)	18 (65)
Race			
White	20	15	26
African American	15	1	1
Asian and others	13		1
Baseline plasma creatinine (mg/dl)	0.88±0.02	1.32±0.1	1.23±0.1
Albumin-to-creatinine ratio (mg/g urinary creatinine)	5.2 (2.09 to 7.5)	71.7 (12.8 to 130.6)	193.7 (118.4 to 269)
Baseline eGFR (ml/min per 1.73 m^2)[a]	93.8±2.6	51.7±3.8	60.1±4.4
Plasma KIM-1 (pg/ml)	64.4 (51 to 77.7)	205.7 (62.15 to 349.3)	1458 (274.8 to 2641)
Urinary KIM-1 (ng/mg urinary creatinine)	0.29 (0.22 to 0.35)	0.77 (0.59 to 0.96)	5.9 (3.21 to 8.70)

Values for continuous variables given as mean±SEM or mean (95% CI). CS, cardiac surgery.
[a]Baseline eGFR was calculated using the Modification of Diet in Renal Disease equation.

J Am Soc Nephrol 25: 2177–2186, 2014.

Original Article

Increased plasma dipeptidyl peptidase 4 activities predict new-onset microalbuminuria in association with its proinflammatory effects in Chinese without diabetes: a four-year prospective study

Tianpeng Zheng[1,2], Attit Baskota[1], Yun Gao[1], Haoming Tian[1] and Fan Yang[2]

[1]Department of Endocrinology and Metabolism, West China Hospital of Sichuan University, Sichuan, P.R. China and [2]Department of Endocrinology and Metabolism, Affiliated Hospital of Guilin Medical University, Guangxi, P.R. China

Nephrol Dial Transplant (2014) 0: 1–7

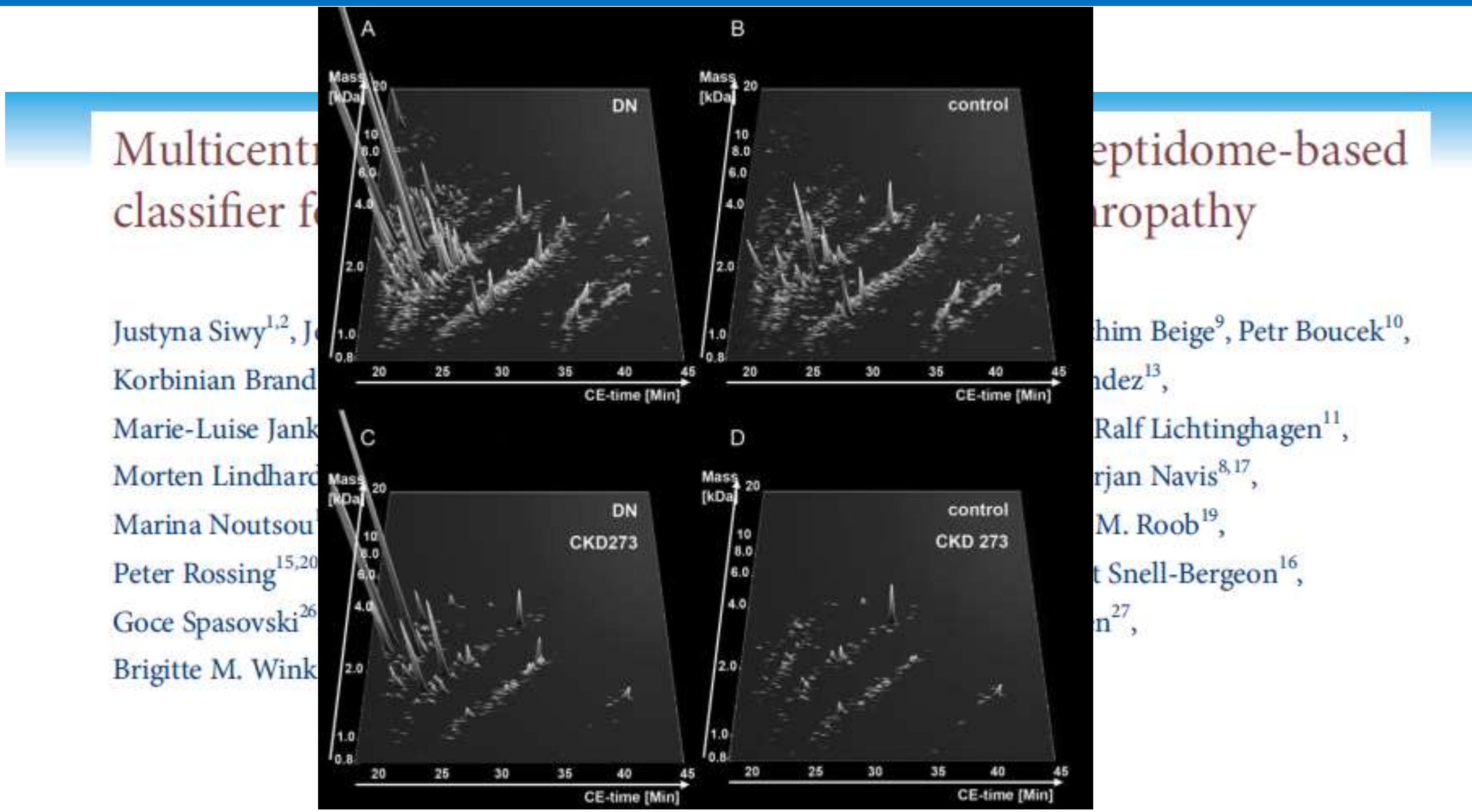
Table 4. Correlation between DPP4 activity and IL-6, hs-CRP, urinary ACR in all participants at baseline and 4 years later

	At baseline				4 years later			
	Univariate[a]		Multivariate[b]		Univariate[a]		Multivariate[b]	
	r	P	*β*	P	*r*	P	*β*	P
Control participants								
IL-6	0.279	0.000	0.230	0.000	0.473	0.000	0.395	0.000
hs-CRP	0.289	0.000	0.231	0.000	0.457	0.000	0.385	0.000
Urinary ACR	0.177	0.000	0.162	0.000	0.222	0.000	0.136	0.000
Case participants								
IL-6	0.543	0.000	0.417	0.000	0.615	0.000	0.560	0.000
hs-CRP	0.346	0.001	0.235	0.013	0.596	0.000	0.550	0.000
Urinary ACR	0.325	0.002	0.214	0.047	0.546	0.000	0.465	0.000
All participants								
IL-6	0.327	0.000	0.257	0.000	0.522	0.000	0.435	0.000
hs-CRP	0.327	0.000	0.246	0.000	0.498	0.000	0.418	0.000
Urinary ACR	0.197	0.000	0.162	0.000	0.383	0.000	0.292	0.000

[a]Pearson's univariate correlation coefficients.
[b]A multivariate regression analysis was performed, after adjustment for age, sex, BMI, WHR, SBP, DBP, FBG, 2 h-PG, fasting insulin, 2 h-insulin, TG, HDL-C, TC, LDL-C, current smoking, alcohol consumption, leisure-time physical activity and family history of diabetes.

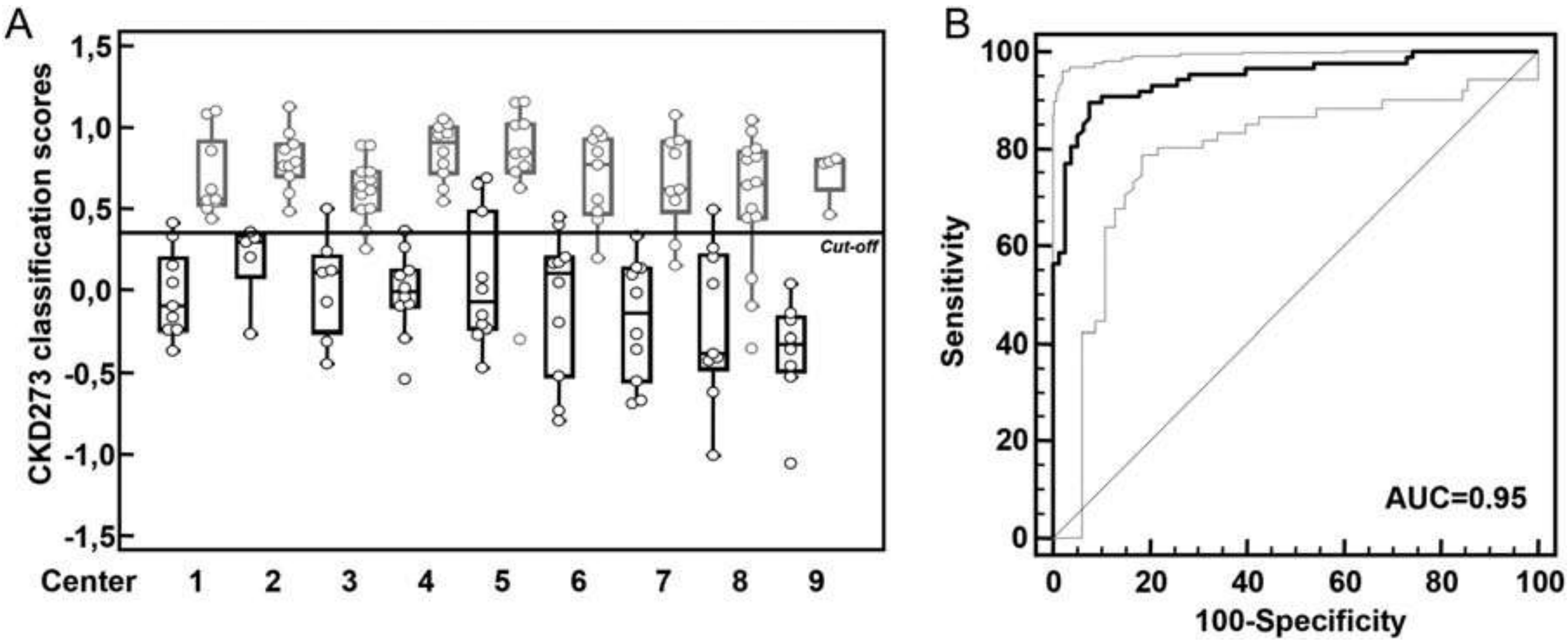
Nephrol Dial Transplant (2014) 0: 1–7

CKD 273 Classifier

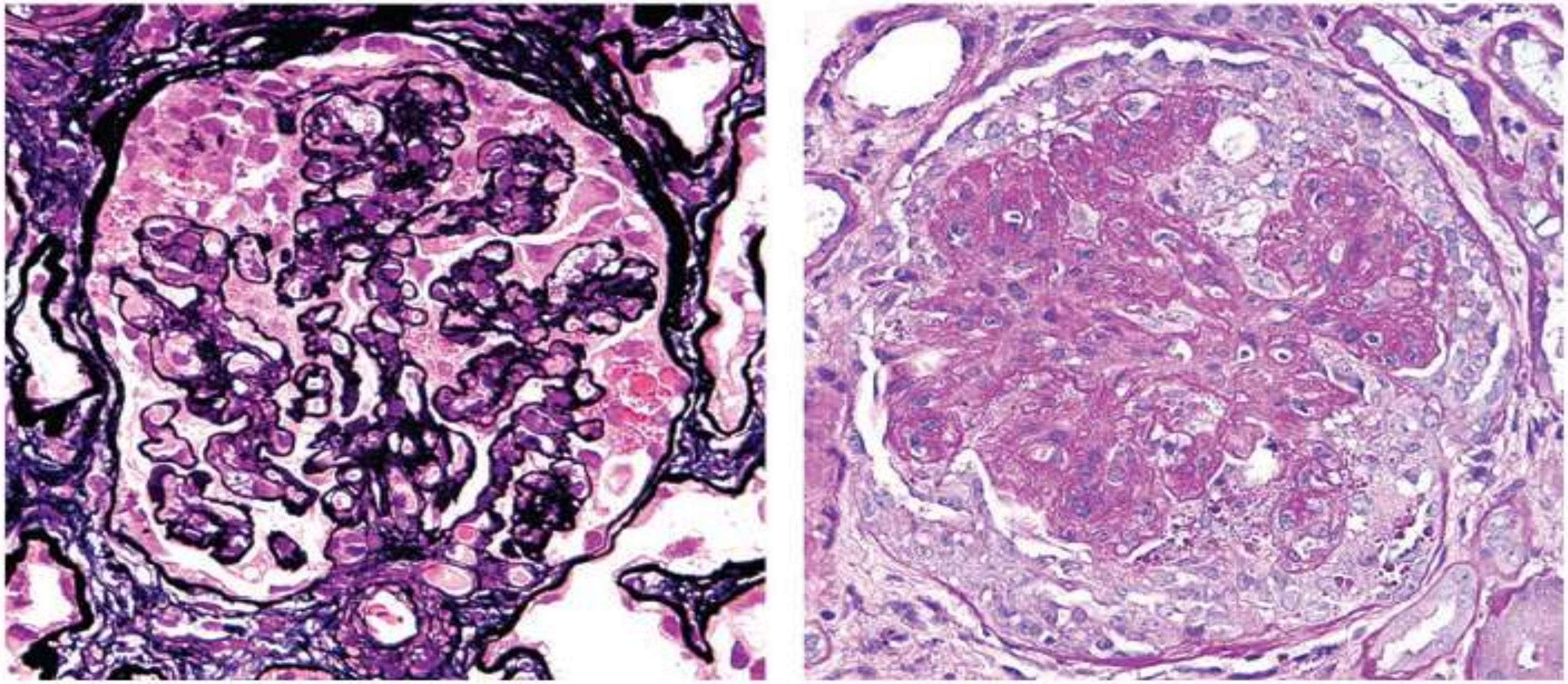


Nephrol Dial Transplant (2014) 29: 1563–1570

CKD 273 Classifier

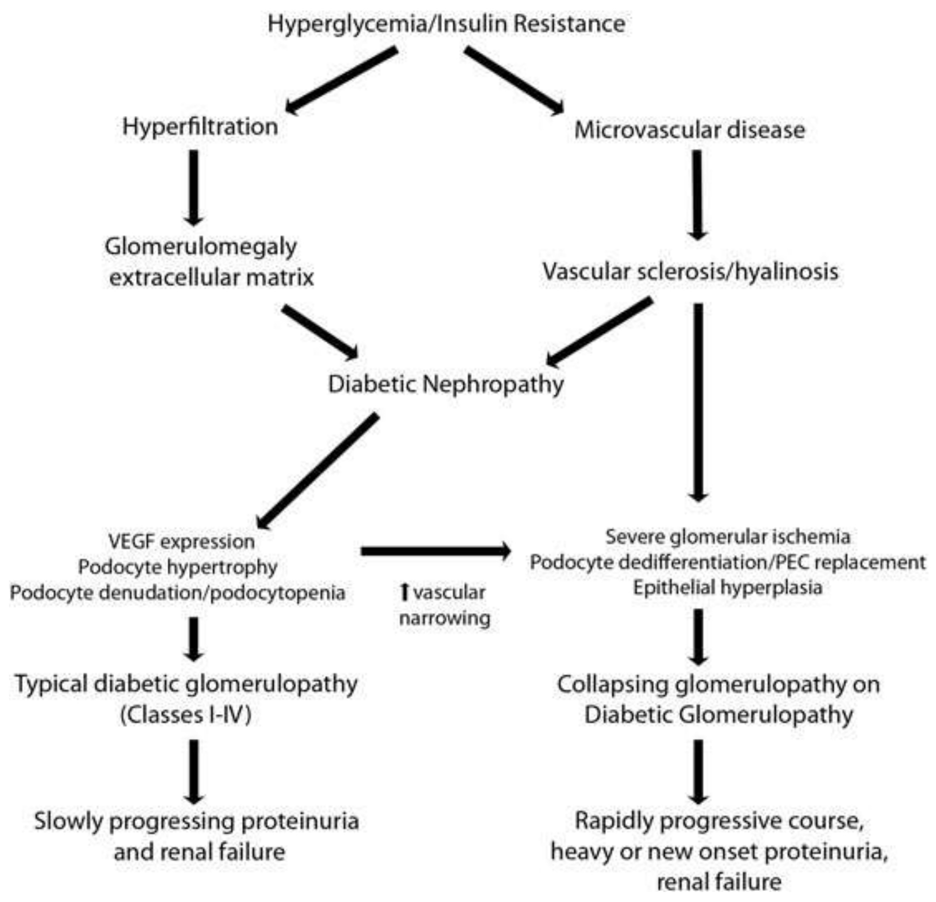


Collapsing GN:
A New Concept

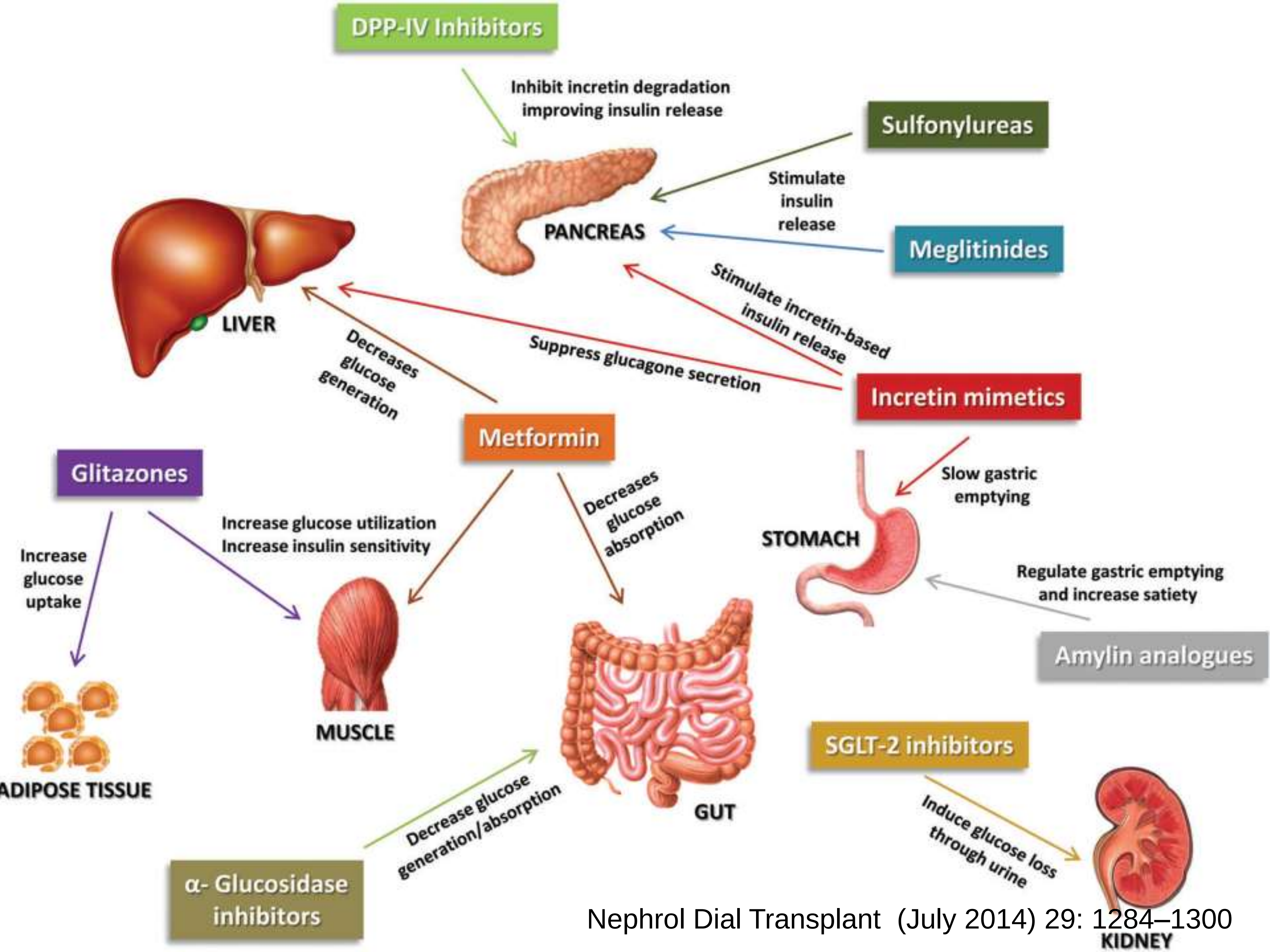


Nephrol Dial Transplant (2014) 29: 392–399

Collapsing GN:
A New Concept



Nephrol Dial Transplant (2014) 29: 392–399



Nephrol Dial Transplant (July 2014) 29: 1284–1300

Oral Antidiabetics

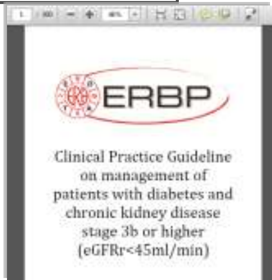
		CKD-1	CKD-2	CKD-3	CKD-4	CKD-5ND	CKD-5D
	Metformin	No adjustments		1,5g-850 mg/day*	500 mg/day**	Consider carefully/Awaiting further data	
Sulfonylureas	Chlorpropamide	No adjustments		100-125 mg/day	To be avoided		
	Acetohexamide	To be avoided					
	Tolazamide	To be avoided					
	Tolbutamide	250mg, 1-3 times/day				To be avoided	
	Glipizide	No adjustments					
	Glicazide	Start at low doses and dose titration every 1-4 weeks					
	Glyburide	To be avoided					
	Glimepiride	Recude dosage to 1 mg/day				To be avoided	
	Gliquidone	No adjustments					
Meglitinides	Repaglinide	No adjustments				Limited experience available	
	Nateglinide	No adjustments				Start at 60 mg/day	To be avoided
α-gluc inhibitors	Acarbose	No adjustments			Avoid if GFR<25mL/min	To be avoided	
	Miglitol	Limited experience available					
	Pioglitazone	No adjustments					
DPP-IV inhibitors	Sitagliptin	No adjustments		Reduce to 50 mg/day	Reduce to 25 mg/day		
	Vildagliptin	No adjustments		Reduce to 50 mg/once daily			
	Saxagliptin	No adjustments		Reduce to 2,5 mg/once daily			
	Linagliptin	No adjustments					
	Alogliptin	No adjustments		Reduce to 12,5 mg/daily			
Incretin Mimetics	Exenatide	No adjustments	Reduce dose to 5 mcg/once to twice daily		To be avoided		
	Liraglutide	Limited experience available					
	Lixisenatide	No adjustments	Careful use if GFR 80-50 mL/min				No experience available
	Pramlintide	Limited experience available					
SGLT-2 inhibitors	Dapagliflozin	Limited experience available					
	Canagliflozin	Reduced efficacy		Careful monitoring		To be avoided	
	Empagliflozin	Limited experience available					

Nephrol Dial Transplant (July 2014) 29: 1284–1300

ERBP

		All cause mortality	Cardiovascular events	Risk of hypoglycaemia	Weight gain	HbA1C change	dose adaptation in CKD stage 3b or higher (eGFR<45ml/min)
Biguanides	Metformin						Yes
Sulfonylureas	Ckoorpropamide						Avoid
	Acetohexamide						Avoid
	Tolazamide						Avoid
	Tolbutamide						Avoid
	Glipizide						no
	Glicazide						Yes
	Glyburide						Avoid
	Glimepiride						Avoid
	Gliquidone						no
Meglitinides	Repaglinide						Yes
	Nateglinide						Yes
a-glucosidase inhibitors	Acarbose						No
	Miglitol						no data
DPP-IV inhibitors	Sitagliptin						Yes
	Vildagliptin						Yes
	Saxagliptin						Yes
	Linagliptin						No
	Alogliptin						Yes
Incretin mimetics	Exenatide						Avoid
	Liraglutide						most likely not
	Lixisenatide						Yes
	Pramlintide						no data
SGLT-2 inhibitors	Dapagliflozin						avoid;not effective
	Canagliflozin						avoid;not effective
	Empagliflozin						avoid;not effective

dark green: evidence for beneficial effect; red: evidence for negative effect; yellow: not investigated or insufficient data; salmon: evidence for weak negative effect; aquamarin: evidence for neutral to weak positive effect; dark blue: evidence for lack of effect/neutral



Gluco-regulatory Hormones: Effect of Dialysis

Original Article

Clearance of glucoregulatory peptide hormones during haemodialysis and haemodiafiltration in non-diabetic end-stage renal disease patients

Morten B. Jørgensen[1], Thomas Idorn[1], Filip K. Knop[2,3], Jens J. Holst[3], Mads Hornum[1] and Bo Feldt-Rasmussen[1]

[1]Department of Nephrology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark, [2]Center for Diabetes Research, Department of Medicine, Gentofte Hospital, University of Copenhagen, Hellerup, Denmark and [3]The NNF Center for Basic Metabolic Research, Department of Biomedical Sciences, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

NDT Advance Access published October 15, 2014

Gluco-regulatory Hormones: Effect of Dialysis

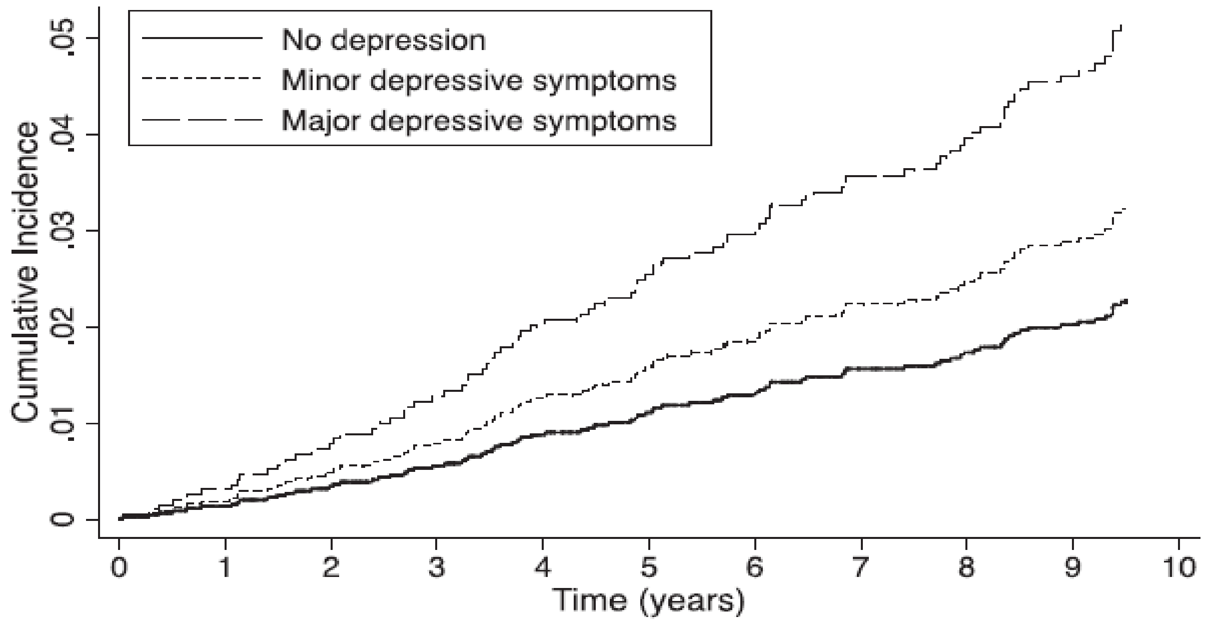
Concentrations during the first hour of dialysis

	0 min	60 min	Decline (%)
Glucose (mmol/L)			
HD	4.9 (4.6–5.3)	4.8 (4.6–5.1)	1.8 (−2.7–6.1)
HDF	5.0 (4.7–5.4)	4.9 (4.6–5.2)	2.9 (−2.1–7.7)
C-peptide (pmol/L)			
HD	2078 (1834–2356)	1163 (987–1371)	44.0 (35.4–51.5)
HDF	1913 (1674–2185)	1065 (891–1273)	44.3 (34.7–52.6)
Insulin (pmol/L)			
HD	44.1 (32.5–59.8)	24.8 (17.2–35.7)	43.7 (30.8–54.3)
HDF	41.4 (30.3–56.6)	24.8 (16.9–36.4)	40.1 (24.5–52.4)
Glucagon (pmol/L)			
HD	66.5 (52.9–83.6)	43.7 (34.7–55.0)	34.3 (27.3–40.7)
HDF	66.0 (52.3–83.2)	35.6 (28.2–44.9)	46.0 (39.6–52.8)[a]
GLP-1 (pmol/L)			
HD	26.8 (20.0–35.9)	20.1 (15.4–26.4)	24.8 (7.0–39.2)
HDF	27.8 (20.4–37.8)	20.8 (15.7–27.5)	25.2 (5.1–41.0)
GIP (pmol/L)			
HD	24.1 (13.8–42.1)	17.6 (10.5–29.5)	26.9 (1.1–45.9)
HDF	26.1 (14.6–46.7)	13.8 (8.2–23.5)	47.0 (25.7–62.1)

NDT Advance Access published October 15, 2014

Outcome

CKD Progression:
Depression and DM

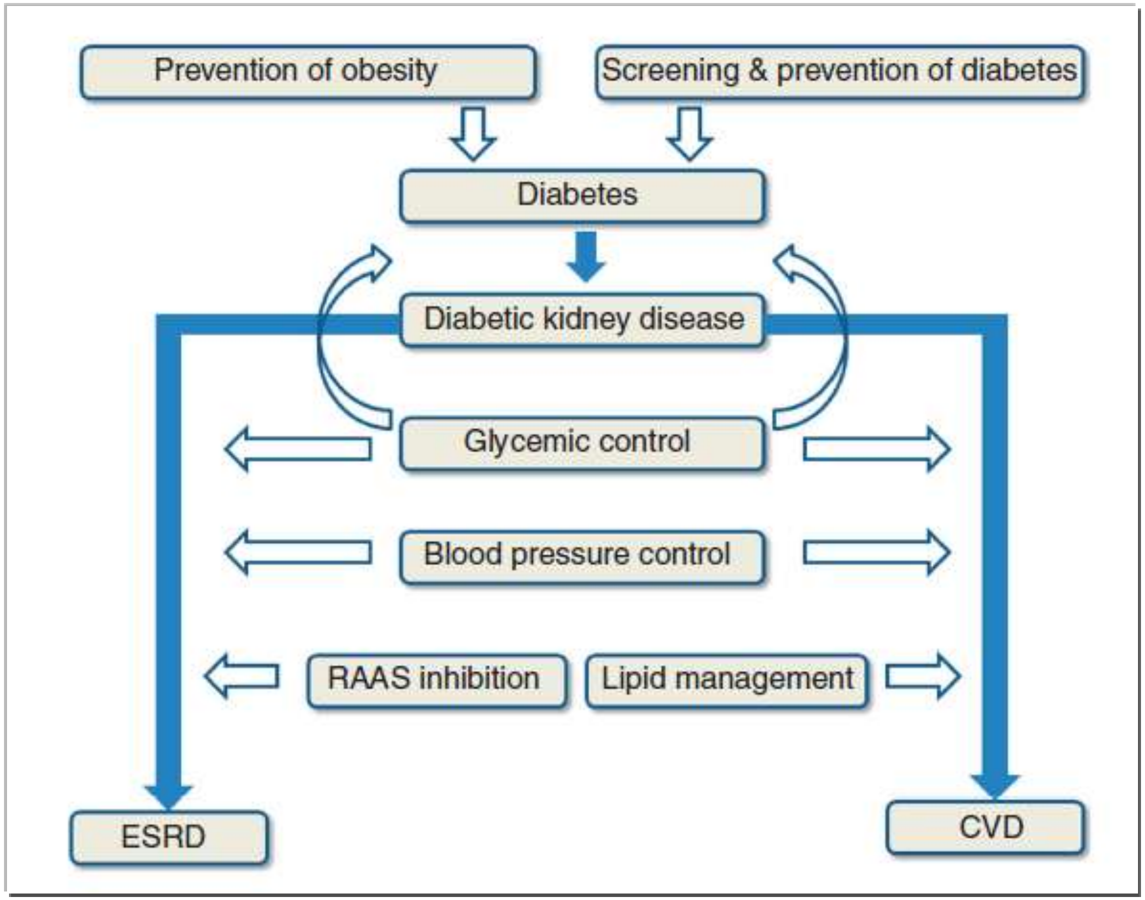


Number at risk

Total	3886	3403	2890	2454	2102
No depression	3111	2756	2365	2026	1743
Minor depressive symptoms	327	277	233	194	157
Major depressive symptoms	448	370	292	234	202

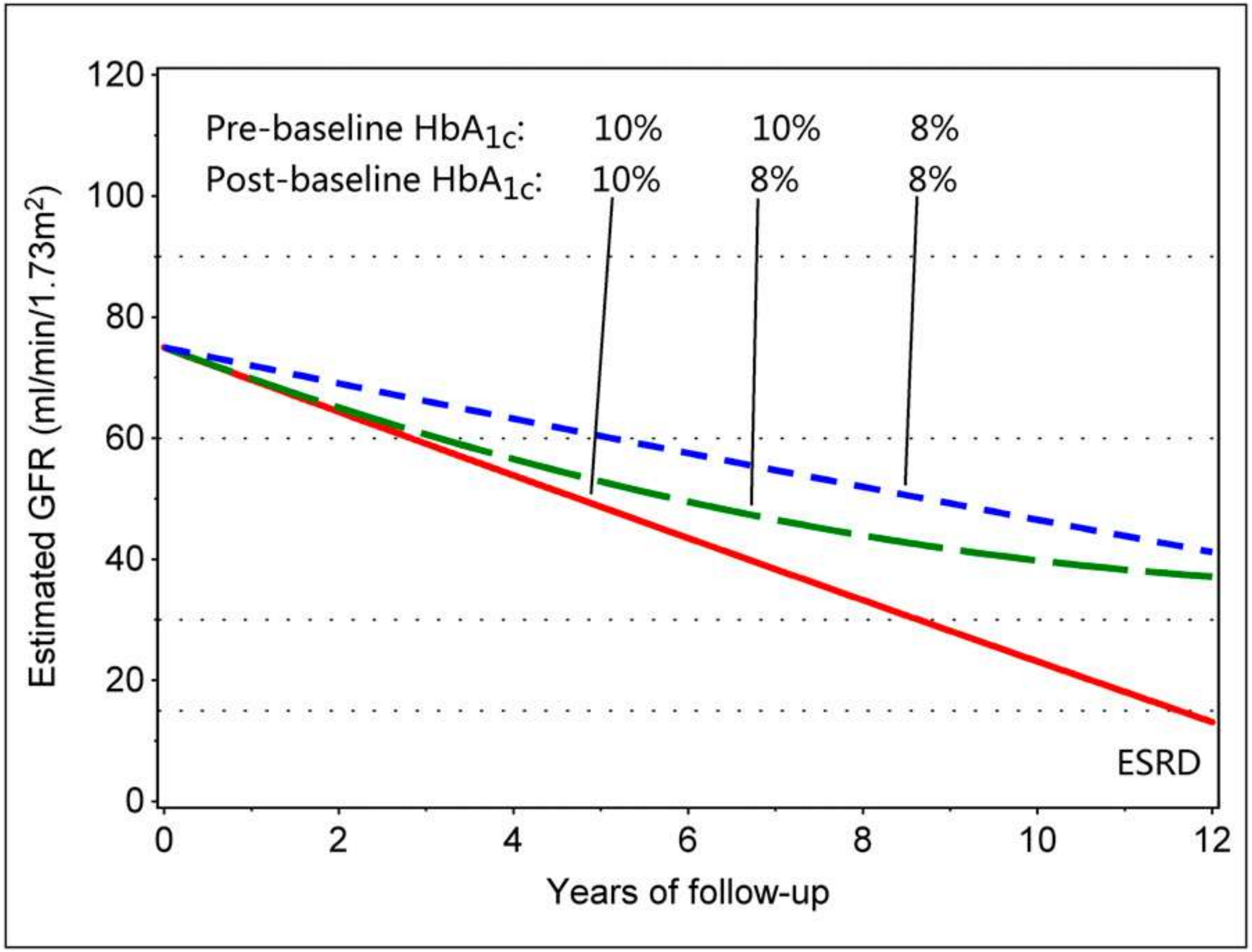
Clin J Am Soc Nephrol 9: 920–928, 2014.

DKD-KDIGO



Kidney International (2015) 87, 20–30

A1c Control:
Risk of ESRD in T1D



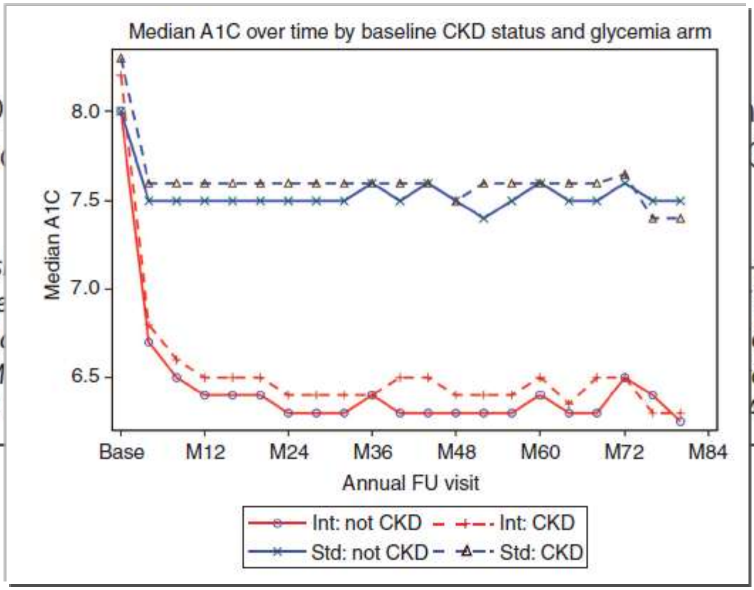
J Am Soc Nephrol 25: 2916–2925, 2014.

A1c Control:
Risk of ESRD in T2D

Chronic kidney disease and intensive glycemic control increase cardiovascular risk in patients with type 2 diabetes

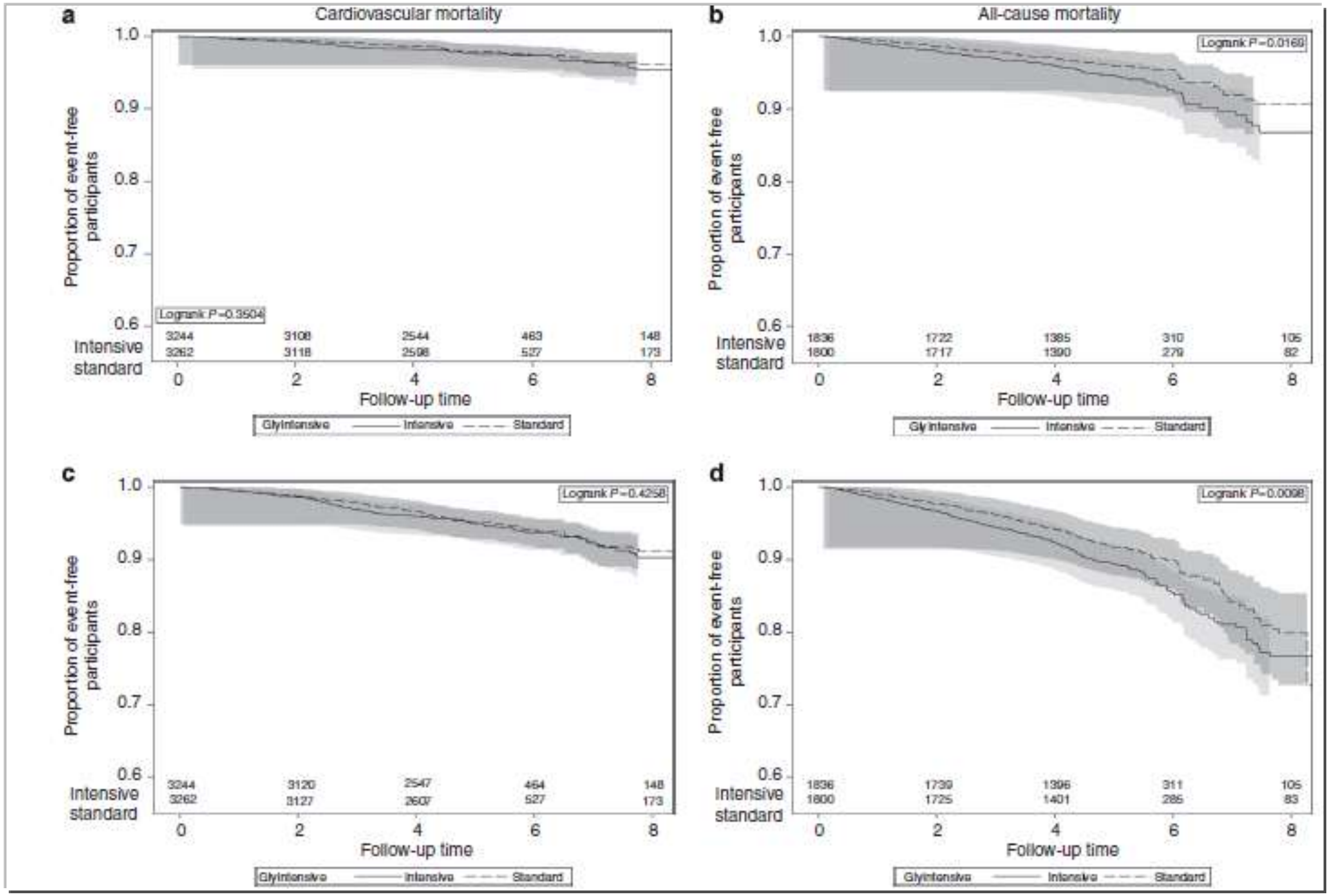
Vasilios Papademetriou[1], Laura Lovato[2], Michael D ... en[5,6],
William B. Applegate[7], Zubin Puntakee[8], Jean Fran ... CORD
Study Group

[1]Veteran Affairs Medical Center and Georgetown University, Was ... -Salem,
North Carolina, USA; [3]Veteran Affairs Medical Center and George ... North
Carolina, Chapel Hill, North Carolina, USA; [5]University of Cincinn ... o, USA;
[7]WFUHS Geriatric/Gerontology, Winston-Salem, Ohio, USA; [8]McM ... oria
Hospital, Barrie, Ontario, Canada and [10]Veterans Affairs Medical ...



Kidney International advance online publication, 17 September 2014

A1c Control:
Risk of ESRD in T2D



Kidney International advance online publication, 17 September 2014

Combined RAS Blockers:
Potassium Story

Article

Potassium Handling with Dual Renin-Angiotensin System Inhibition in Diabetic Nephropathy

Peter N. Van Buren,† Beverley Adams-Huet,† Mark Nguyen,* Christopher Molina,* and Robert D. Toto*†*

Clin J Am Soc Nephrol 9: 295–301, 2014.

Outcome in T1D:

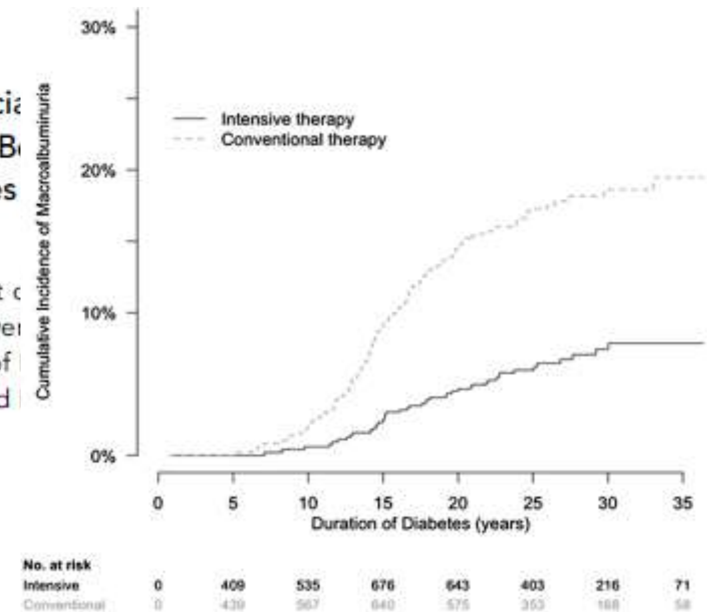
Effect of Macroalbuminuria

CLINICAL EPIDEMIOLOGY www.jasn.org

Renal Outcomes in Patients with Type 1 Diabetes and Macroalbuminuria

Ian H. de Boer,* Maryam Afkarian,* Tessa C. Rue,† Patricia
Mark E. Molitch,§ Michael W. Steffes,‖ Wanjie Sun,‡ and B
Control and Complications Trial/Epidemiology of Diabetes
(DCCT/EDIC) Research Group

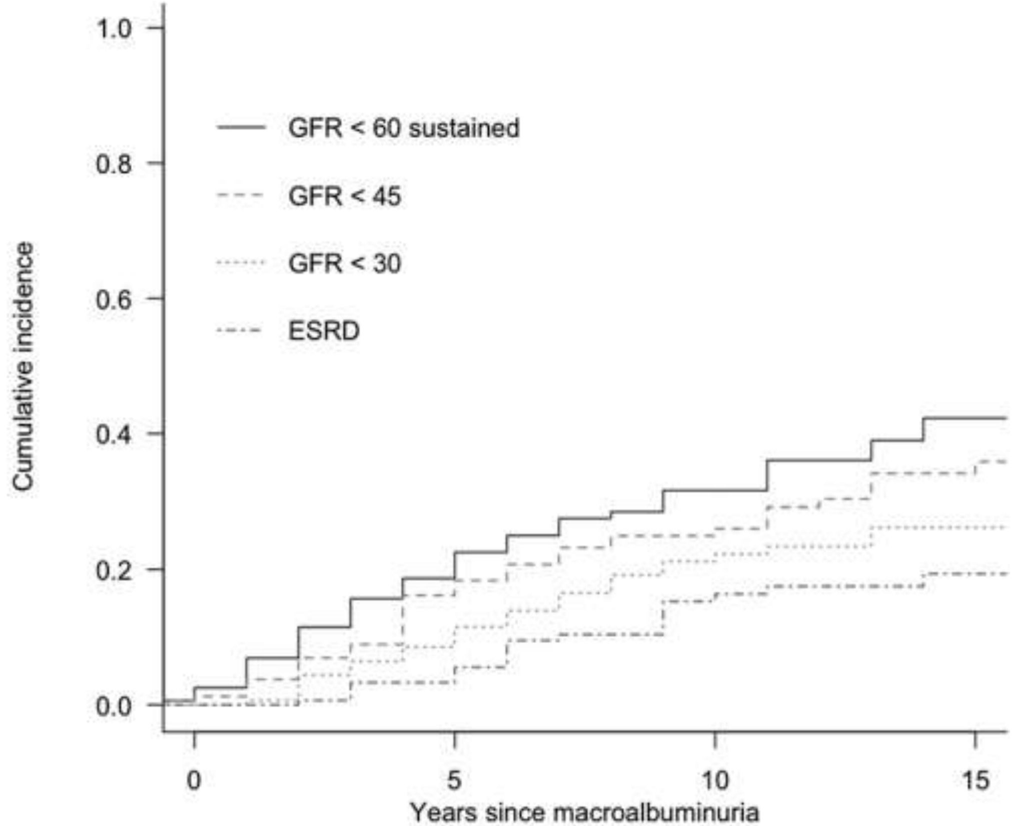
*Division of Nephrology and Kidney Research Institute and †Department
Seattle, Washington; ‡Biostatistics Center, The George Washington Unive
Endocrinology, Northwestern University, Chicago, Illinois; ‖Department of
University of Minnesota, Minneapolis, Minnesota; and ¶Samuel Lunenfeld
University of Toronto, Toronto, Ontario, Canada



J AmSoc Nephrol 25: 2342–2350, 2014

Outcome in T1D:

Effect of Macroalbuminuria



No. at risk

GFR < 60 sustained	154	99	61	30
GFR < 45	158	110	69	36
GFR < 30	159	119	70	37
ESRD	159	125	75	37

J AmSoc Nephrol 25: 2342–2350, 2014

Consensuses and Guidelines

DKD:
A Report From ADA

Box 2. Other Cause(s) of CKD Should Be Considered in the Presence of Any of the Following Circumstances

- Absence of diabetic retinopathy;
- Low or rapidly decreasing GFR;
- Rapidly increasing proteinuria or nephrotic syndrome;
- Refractory hypertension;
- Presence of active urinary sediment;
- Signs or symptoms of other systemic disease; or
- $>$30% reduction in GFR within 2-3 months after initiation of an ACE inhibitor or ARB.

Am J Kidney Dis. 2014;64(4):510-533

DKD:
A Report From ADA

Hypertension	Goal BP is <140/80 mm Hg Treatment consists of lifestyle modifications and oral medications that generally should include RAAS blockers	Goal BP is <140/90 mm Hg Goal BP is 30 mg/g creatinine Goals for treatment are based primarily on studies of patients with nondiabetic CKD Treatment consists of lifestyle modifications and oral medications that usually include RAAS blockers Use of more than one RAAS blocker should generally be avoided

Am J Kidney Dis. 2014;64(4):510-533

Guidelines:
Statins in CKD

EDITORIAL www.jasn.org

We Don't Prescribe Statins to Lower Cholesterol: We Prescribe Statins to Reduce Vascular Risk

Marcello Tonelli
Department of Medicine, University of Calgary, Calgary, Alberta, Canada

J Am Soc Nephrol 26: 2015 in press

Guidelines:
2014 BP Guidelines

CLINICAL COMMENTARY www.jasn.org

Commentary on the 2014 BP Guidelines from the Panel Appointed to the Eighth Joint National Committee (JNC 8)

Efrain Reisin,* Raymond C. Harris,[†] and Mahboob Rahman[‡]

*Section of Nephrology and Hypertension, Louisiana State University Health Science Center, New Orleans, Louisiana; [†]Division of Nephrology, Vanderbilt University School of Medicine, Nashville, Tennessee; and [‡]Division of Nephrology and Hypertension, Case Western Reserve University, University Hospitals Case Medical Center, Louis Stokes Cleveland VA Medical Center, Cleveland, Ohio

Guideline	Younger Target (mmHg)	Older Target (mmHg)	Diabetes Target (mmHg)	CKD Target (mmHg)
2014 Evidence-Based Guidelines for the Management of High Blood Pressure	<140/90	>60 years of age: <150/90	<140/90	<140/90

J Am Soc Nephrol 25: 2419–2424, November 2014

ERBP

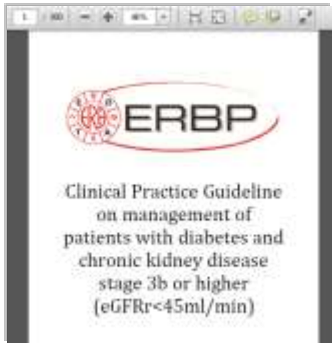
Chapter 1.1. Should patients with diabetes and CKD stage 5 start with peritoneal dialysis or haemodialysis as a first modality?

Dialysis modality choice in diabetic patients with end-stage kidney disease: a systematic review of the available evidence

Cecile Couchoud[1], Davide Bolignano[2,3], Ionut Nistor[4], Kitty J. Jager[5], James Heaf[6], Olle Heimburger[7] and Wim Van Biesen[8] on Behalf of the European Renal Best Practice (ERBP) Diabetes Guideline Development Group

[1]REIN registry, Agence de la biomédecine, Saint-Denis La Plaine, France, [2]CNR-Institute of Clinical Physiology, Reggio Calabria, Italy, [3]ERBP, Ghent University Hospital, Ghent, Belgium, [4]Nephrology Department, Gr. T. Popa University of Medicine and Pharmacy, Iasi, Romania, [5]ERA-EDTA Registry, Department of Medical Informatics, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands, [6]Department of Nephrology B, Copenhagen University hospital at Herlev, Herlev, Denmark, [7]Division of Renal Medicine, Department of Clinical Science, Karolinska Institutet, Huddinge University Hospital, Stockholm, Sweden and [8]Chair of ERBP, Renal Division, Ghent University Hospital, Ghent, Belgium

Nephrol Dial Transplant (2014) 0: 1–11

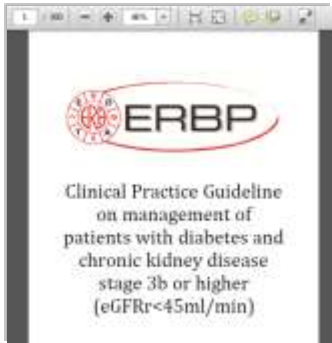


ERBP

Chapter 1.2: Should patients with diabetes and CKD stage 5 start dialysis earlier, i.e. before becoming symptomatic, than patients without diabetes?

Statements

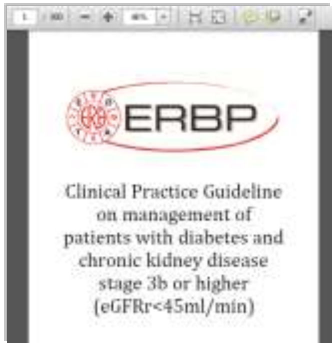
1.2.1 We recommend to initiate dialysis in patients with diabetes on the same criteria as in patients without diabetes (**1A**)


ERBP

Clinical Practice Guideline on management of patients with diabetes and chronic kidney disease stage 3b or higher (eGFRr<45ml/min)

ERBP

Chapter 1.3: In patients with diabetes and CKD stage 5, should a native fistula, a graft or a tunnelled catheter be preferred as initial access?



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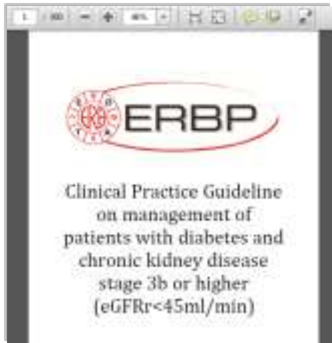
chapter 1.4 Is there a benefit to undergo renal transplantation for patients with diabetes and CKD stage 5?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Clinical Practice Guideline
on management of
patients with diabetes and
chronic kidney disease
stage 3b or higher
(eGFRr<45ml/min)